

of 4 to 23 amino acids around the cleavage site blocked shedding of the human FasL from the membrane while the apoptosis-inducing activity was retained. Mouse WR19L cells overexpressing the Fas is sensitive to membrane-bound FasL as in the case with the FasL of soluble form whereas Jurkat cells and mouse primary hepatocytes which endogenously express a low level of Fas exhibited resistance to soluble FasL. When the membrane-bound FasL was used as an effector, the human Jurkat cells and the mouse hepatocytes were efficiently killed. Furthermore, soluble FasL inhibited cytotoxicity of the membrane-bound FasL to the mouse hepatocyte. These results indicate that the membrane-bound form of FasL is the functional form, and its activity is downregulated by the shedding of the soluble FasL from the membrane.--

The paragraph beginning on page 7, line 16 should be replaced with the following paragraph:

--FIG. 2 is a schematic diagram of the FasL constructs carrying deletion or point mutation.--

The paragraph beginning on page 11, line 14 should be replaced with the following paragraph:

--It should be noted that the amino acid sequences shown in SEQ ID No. 1 and 2 have four glycosylation sites (N-glycosylation sites), respectively. In SEQ ID No. 1, amino acid numbers 76 - 78, 161 - 163, 227 - 229, and 237 - 239, and in SEQ ID No. 2, amino acid numbers 76 - 78, 180 - 182, 246 - 248, and 256 - 258

*cn<sup>2</sup>* *C<sub>3</sub>* correspond to such glycosylation sites. The novel FasL derivative of the present invention may also have a sugar chain added thereto at such site.--

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The paragraph beginning on page 13, line 12 should be replaced with the following paragraph:

*C<sub>4</sub>* --The soluble Fas ligand of the present invention is the ligand which shares at least some region with the natural Fas ligand; which is soluble in an aqueous solution in the absence of a surfactant; and which interacts with the extracellular region of the Fas to compete with the natural FasL or to induce downregulation of the Fas. Exemplary such soluble Fas ligand is the one comprising at least some of the extracellular region of the Fas ligand, and a preferable example of the soluble Fas ligand is a polypeptide comprising the amino acid sequence of human natural Fas ligand from Gln 130 from N terminal to the C terminal.--

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The paragraph beginning on page 15, line 9 should be replaced with the following paragraph:

*C<sub>5</sub>* --Exemplary heart diseases include ischemic heart diseases such as myocardial infarction, myocarditis of various causes, cardiomyopathy, in particular, dilated cardiomyopathy, cardiac insufficiency, and ischemic reperfusion injury and diseases caused by such ischemic reperfusion injury. Exemplary GVHD include GVHD after bone marrow transplantation such as incompatible bone marrow

transplantation and bone marrow transplantation in the case of congenital immunodeficiency; GVHD after organ transplantation; GVHD after blood infusion of large amount to the host with reduced immunocompetence. Ischemic reperfusion injuries include ischemic reperfusion injuries found in liver, heart, kidney, lung, spleen, small intestine, large intestine, stomach, pancreas, brain, muscle, skin, and the like as well as diseases caused by such ischemic reperfusion injury such as hepatic insufficiency, reperfusion arrhythmia, renal insufficiency, necrotizing enterocolitis, and other injuries and dysfunction of various organs.--

IN THE CLAIMS

Please cancel claims 1 and 7 without prejudice or disclaimer of the subject matter contained therein.

Please replace claims 2-6 with the following amended claims.

2. A novel polypeptide having an amino acid sequence of natural human Fas ligand wherein the 129<sup>th</sup> amino acid and 130<sup>th</sup> amino acid residues as measured from N terminal end are both deleted or substituted, and at least one amino acid residue of from 111<sup>th</sup> amino acid to 128<sup>th</sup> amino acid residues or at least one amino acid residue of from 131<sup>st</sup> amino acid to 133<sup>rd</sup> amino acid residues as measured from N terminal end is deleted or substituted.